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The TNM classification of malignant tumours—towards common understanding and reasonable expectations

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Clarity and precision about the anatomical extent of disease in cancer is essential for prognostication, research, and cancer-control activities. Although the addition of predictive markers, molecular and genomic profiling, and imaging data has contributed important advances to the care of cancer patients, it has also complicated the clarity of the purpose and mission of cancer staging. We believe that communication of the core purpose of the Tumour, Node, Metastasis (TNM) classification to different audiences, to address uncertainty about its application and to articulate the future of this system to permit ongoing study of factors that underpin most cancer discoveries, is urgently needed.

The TNM classification provides a synoptic structure for communication about cancer disease extent and has been a cornerstone of cancer care and research for decades. It is an integral part of the cancer language;^{1,2} however, its purpose, scope, and application warrant clarification to enable maximal benefit for patients and for global cancer control.

The TNM classification has many purposes: in cancer control (specifically surveillance at the population level),^{3,4} in research activity (clinical trials eligibility and stratification, translational research), and as a framework to guide clinical care and decision making in addition to communicating prognosis.⁵ The TNM classification therefore attempts to convey a picture of the anatomical extent of disease to multiple user groups in a manner that accommodates their diverse needs. These purposes need to be applied in many jurisdictions, environments, and among different specialties in a consistent manner if the goal of a worldwide language to describe disease extent is to be achieved. As frequently happens with

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any language, the interpretation of definitions and terms has strayed from the original intention. Moreover, the universal use of the TNM classification has made it a subject of unreasonable expectation. For example, suggestions have been made that TNM needs to serve many additional purposes, such as encompassing all prognostic factors, or becoming a repository to record all attributes encompassed in a synoptic pathology report. Even in this context, the emphasis appears unbalanced with a bias towards the inclusion of tumour biology rather than other important elements such as patient factors (age, performance status, or comorbidity) and treatment variables.

When it was originally developed, the TNM classification was designed and intended to depict the anatomical burden of cancer in individuals or groups of patients and was not explicitly intended for other purposes. The limitations of TNM were recognised at its genesis with the acknowledgment that many factors in addition to TNM contribute to prognosis (including age, sex, and numerous histopathological attributes including grade).^{6,7} Nonetheless, the simplicity and ease of use of the TNM classification by clinicians led to its ubiquitous adoption worldwide. To maintain expediency and convenience, it is understood that the TNM classification cannot be expected to be perfect, but as a compromise between the ideal and the practical, it has demonstrated enduring applicability for worldwide use. The use of the TNM classification in the cancer surveillance community, and particularly population-based cancer registries, has evolved, necessitating simplification that permits comparability at the population level, a crucial element to evaluate cancer control measures.

TNM classification was not intended to address tumour biology, or patient or environmental factors that determine access or quality of treatment. Nonetheless, although it does reflect prognosis, TNM does not meet all prognostic needs.⁸ In isolated cases, tumour grade (sarcoma) and age (thyroid) were included historically to define categories or stage. Ironically, the absence of an alternative universally available framework for prognostic classification has incited frequent requests for a change in the purpose of TNM.

To better define the principles of the TNM classification, a Global Consultation on Cancer Staging was held under the auspices of the Union for International Cancer Control (UICC) and *The Lancet Oncology* with support from the US National Cancer Institute (NCI) and the US Centers for Disease Control and Prevention (CDC). We brought together experts from the UICC, AJCC (American Joint Commission on Cancer), NCI, CDC, Fédération Internationale de Gynécologie et d'Obstétrique (FIGO), International Association of Cancer Registries (IACR), International Agency for Research in Cancer (IARC), and the International Collaboration on Cancer Reporting (ICCR). We had discussions about the challenges in reaching a common understanding of cancer staging and the needs of the different stakeholders. We reaffirmed the purpose of staging classification, recognised the scope of TNM, and provided guidance for its appropriate use.

In the future, attention to strategies and systems is needed to develop sound prognostic classifications that would allow inclusion of all relevant factors, including TNM, in a manner sensitive to the state of knowledge and availability of new treatments. Such models could involve important statistical methods such as parameter estimates, competing risk assessment, sensitivity analysis, and validation, while also recognising limitations in their

use. They should also respond to the needs of personalised approaches and embody the newest technologies, such as artificial intelligence and neural networks that can be used to predict outcomes in individual cancer patients. The AJCC has already taken strides in these initiatives⁸ and attendees of the Consultation agreed that the next steps for the consultation group need to develop processes to identify essential prognostic factors to be included in such models. Strategies will also concentrate on the identification of necessary data elements for collection by cancer registries throughout the world, while developing tools to combine all prognostic factors relevant to personalised patient care.

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